methods to execute functions, which are controlled by damaged brain regions. A special focus will be given on adaptive difficulty levels, allowing error-free learning that is expected to increase motivation, fun, and self-confidence. The "robot-programming-as-cognitive-training" approach aims to explore the impact that the activity of programming a friendly robot might have on AD and MCI patients' condition. Overall the major research questions that we pose are: (a) how to develop a programming task protocol that could reliably help identifying patients' level of cognitive impairment; (b) what is the long-term impact of engaging patients in robot programming activities; (c) how to develop engaging game-like software to help patients easily practice programming activities; and (d) exploring the usability issues of different interface modalities (tangibles vs. GUIs) when used to program the robot (we use Lego NXT robots)(http://aspad.csd.auth.gr). Long Lasting Memories (LLM; www.longlastingmemories.eu) was a European project aiming to improve elderly individuals' cognitive abilities through specialized mental and physical exercises. Funded by the European Commission, it involved 12 participating research teams, from 6 different European countries. Data collected in extensive LLM trials reveal the (rather unspecific) influence of exercise dosage, age, cognition and social activity level on the exercise-induced cognitive effects.Education and training for all stakeholders (i.e. health professionals and informal and formal caregivers) through distance education platforms and e-collaboration services. To augment this effort, the research team integrates biofeedback modules for stress measurement in teleconferences in order to support the emotional awareness of the participants. (http://aspad.csd.auth.gr). The results of LLM as well as other technological interventions are utilised as experiential learning material for a distance learning course on elderly carers. This is another EC funded project named DISCOVER (www.discover4carers.eu), in which several partners are collaborating on finding the best ICT solutions to support people in their caring roles. Finally, Symbiosis is a revolutionary system aiming at providing integrated solutions to a series of problems related with Alzheimer. It is the first integrated Alzheimer support system that takes into account patient's response in an adaptive way that fulfills each patient's special needs and provides to caregivers and doctors considerable facilitations, unlocking the potential of innovative supporting role. Caregivers use Symbiosis as an information source about the status of their AD patients and as a means to come even closer by sharing and discussing related problems with a broader community. Physicians handle more AD patients and monitor them more closely, increasing their awareness and their assistive intervention in the AD patients' living. Finally, Symbiosis introduces a new market environment by providing the SymbiosisNet that supports a network of plug-in apps from third-party developers (e.g., young programmers) towards expansion and increased functionality. www.youtube.com/watch?v=BDkLz-T-jYE

TAU AS A MOLECULAR BIOMARKER IN CEREBROSPINAL FLUID AND PLASMA

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Recent experimental evidence has demonstrated that tau protein and abnormal tau aggregates might display a prion-like behavior in neurodegenerative diseases and there is an emerging interest in tau-focused drug candidates, such as tau immunotherapy. Progress on development of tau selective PET radioligands together with assays measuring the levels of tau in cerebrospinal fluid (CSF) and plasma/serum make these tau biomarkers prime candidates to guide and facilitate drug development. Our current knowledge on CSF-tau has led to internationally recognized efforts with the aim to develop analytically and clinical/biological validated assays. Besides CSF, pathological changes in the brain are also reflected in plasma/serum as suggested by clinical studies. Technological advances such as a superconducting quantum interference device (SQUID), immuno-magnetic reduction (IMR) and single molecule detection, via e.g. the SIMOA technology by Quanterix, have made it possible to quantify the low endogenous levels of tau in plasma/serum. However, the absence of a clear correlation between tau-levels in plasma and CSF in AD patients, demonstrate that we are still in the early stages of our understanding of plasma-tau as a marker for brain-specific pathological processes. Finally, mechanistic insights from tau drug candidates in model systems will lead to omics-based multi-analyte assays in plasma. Combined tau and omics-based tests can then be used in well-designed clinical trials to advance new tau drugs into clinically relevant patient management.

Keywords. Tauopathy, Biomarker

THE ROLE OF EEG IN CLINICAL TRIALS ON ALZHEIMER'S DISEASE

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Until recently, phase III double-blind randomized controlled clinical trials of interventions in Alzheimer's disease (AD) have not included investigations other than the cognitive and behavioral assessments, although many studies have reported a potential role for biomarkers. Lately, some clinical trials have implemented biomarkers as secondary outcome measures to support the clinical treatment effect. One of these biomarkers is electroencephalography (EEG), which displays electrical brain activity in relation to neurological disorders. EEG has several favorable properties: It exerts a limited burden on the patients, is relatively cheap to perform, is stable over time, and can be transferred quickly between centers for central assessment. From a technical point of view, EEG has the advantage of a high temporal resolution which allows for the assessment of dynamic processes in the brain. It provides the basis for a vast number of possible signal analyses of which functional brain connectivity and network analyses have gained interest in the last years. Disadvantages include the limited spatial resolution and the specialized training that is needed for analysis and interpretation. In AD, EEG changes include slowing of the dominant oscillation frequency, a reduction of functional connectivity strength and a change of the functional brain networks in the direction of a more chaotic and random organization. Despite these findings, EEG as a research tool in clinical trials has not yet been fully developed. In this presentation, several reasons for this paradox are discussed, as well as some potential approaches to increase the use of EEG in AD related clinical trials. An example of implementation of EEG in a clinical trial, the Souvenir II trial of the effect of the medical food Souvenaid on cognition and EEG in mild AD patients, will be presented.

Keywords. EEG, Biomarker, Clinical trial

BACE1 INHIBITION AS A THERAPEUTIC STRATEGY FOR ALZHEIMER'S DISEASE

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The beta-amyloid (Abeta) peptide is the major constituent of amyloid plaques in Alzheimer's disease (AD) brain and is likely to play a critical early role in the pathogenesis of this devastating neurodegenerative disorder. The beta-secretase, beta-site amyloid precursor protein cleaving enzyme 1 (BACE1; also called Asp2, memapsin 2), is the enzyme responsible for initiating the generation of Abeta in the brain. Thus, BACE1 is a prime drug target for the therapeutic inhibition of Abeta production for the treatment and prevention of AD. Indeed, several pharmaceutical companies have recently launched clinical trials of small molecule BACE1 inhibitor drugs in humans. Since its discovery over 14 years ago, much has been learned about the normal function of BACE1 and its pathophysiological role in AD. This seminar will review BACE1 properties, physiological functions, and dysregulation in AD. Recent discoveries of novel BACE1 substrates and their physiological roles will also be discussed. Finally, the therapeutic potential of BACE1 inhibitors for AD will be considered.

Keywords. BACE1, beta-secretase, Abeta

PREVENTIVE DRUG TRIALS FOR ALZHEIMER'S DISEASE.

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